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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,289	05/31/2002	Vega Masignani	PP01639.102; 2300-1639	6882

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,289	MASIGNANI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,9,10,13,15,17,19,21 and 23-33* is/are pending in the application.

4a) Of the above claim(s) *7,9,13,15,17,19,21,23,24 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10 and 25-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *41403*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence search report (one)*.

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 01/14/02 and 11/08/04. With at least one of these, Applicants have amended the specification.

Election

2) Acknowledgment is made of Applicants' election filed 11/08/04, with traverse, of invention I, claims 1 and 10, drawn to a polypeptide, in response to the written lack of unity mailed 05/07/04. Applicants state that they have elected the species, SEQ ID NO: 1331, amino acids 959-976 of ORF 114-1, allegedly in response to the species election requirement. Applicants' traversal is on the grounds that the claims as amended currently pertain to the same elected species, i.e., the peptides including SEQ ID NO: 1331, which is the special technical feature. Applicants submit that PCT Rule 13.2 permits the product of invention I and the method of using the product of invention IV to be examined together, 'if they distinguish over the art'.

Applicants' arguments have been carefully considered, but are non-persuasive. Contrary to Applicants' assertion and as explained in the written lack of unity mailed 05/07/04, the instruction to further elect one SEQ ID number was not to be construed as a species election. No species election requirement was made in the instant application. Applicants are correct in that PCT Rule 13.2 permits the claims drawn to the product and the method of using the product to be examined together. However, in the instant application, the product is already disclosed in the prior art (see the art rejections set forth below), and therefore the special technical feature is not a unifying feature. For this reason, the lack of unity set forth is proper and is hereby made FINAL.

Status of Claims

3) Claims 5, 11 and 12 have been canceled via the amendment filed 01/14/02.

Claims 1, 3, 4, 6, 7, 9 and 10 have been amended via the amendment filed 01/14/02.

New claims 14-24 have been added via the amendment filed 01/14/02.

Claims 2-4, 6, 8, 14, 16, 18, 20 and 22 have been canceled via the amendment filed 11/08/04.

Claims 1, 7, 9, 10 and 24 have been amended via the amendment filed 11/08/04.

New claims 25-33 have been added via the amendment filed 11/08/04.

Claims 1, 7, 9, 10, 13, 15, 17, 19, 21 and 23-33 are pending.

Claims 7, 9, 13, 15, 17, 19, 21, 23, 24 and 33 have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1, 10 and 25-32 are under examination. A First Action on the Merits is issued for these claims.

Sequence Listing

4) The raw sequence listing submitted in this application has been entered on 08/14/2002.

Information Disclosure Statement

5) Acknowledgment is made of Applicant's Information Disclosure Statement filed 04/14/03. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Priority

6) This instant application is the national stage 371 application of the international application PCT/IB00/01026 filed 07/13/2000 and claims foreign priority to application, 9916529.2, filed 07/14/1999 in United Kingdom.

It is noted that Applicants have submitted a certified copy of the foreign priority document on 01/14/02.

Specification - Informalities

7) The specification of the instant application is objected to for the following reasons:

(a) The use of trademark recitations in the instant specification has been noted. For example, see first full paragraph on page 24: 'Tween 80' and 'Span-85'. The recitations should be capitalized wherever they appear or be accompanied by the generic terminology. See M.P.E.P 608.01(V) and Appendix l. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to trademark recitations, wherever such recitations appear.

(b) On page 28, line 3, and page 26, lines 21 and 22, the address of the American Type Culture Collection is incorrect. Effective 23 March 1998, ATCC has a new address: 10801

University Boulevard, Manassas, VA 20110-2209. Amendments to the specification are suggested to reflect this. It is suggested that Applicants examine the whole specification to make similar correction to the address, wherever it appears.

Rejection(s) under 35 U.S.C § 101

8) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

9) Claim 1 and those claims that depend therefrom are rejected under 35 U.S.C § 101 as being directed to a non-statutory subject matter.

Claim 1 is drawn to a polypeptide, and therefore reads on products of nature, i.e., naturally occurring polypeptide. The claim lacks limitations which distinguish this product from those that may exist naturally for example on the surface of a naturally existing *Neisseria*. Consequently, the claim does not embody patentable subject matter as defined in 35 U.S.C § 101. See MPEP 2105. The rejection can be obviated by amending claim 1 to recite --An isolated .... polypeptide-- in connection with the product to reflect the hands of the inventors in the production or creation of the recited product if descriptive support exists in the specification, as originally filed, for such a limitation.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

10) Claim 1 and those dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The base claim 1 includes the new limitation: a polypeptide comprising 'a contiguous amino acid sequence with at least 50% sequence identity to SEQ ID NO: 1331'. Applicants refer to page 2, lines 1 and 2 of the specification for descriptive support for the amendments introduced to claim 1. However, there appears to be no descriptive support for this new limitation in the specification, as originally filed for the limitation(s) identified above. Therefore, the above-identified limitation in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific

percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C. § 112, First Paragraph (Written Description)

11) Claims 1, 10 and 25-32 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

It is noted that the claimed polypeptide comprising a contiguous amino acid sequence with at least 50% sequence identity to SEQ ID NO: 1331 (i.e., a polypeptide variant having 50% to 99% identity to SEQ ID NO: 1331) does not exist independent of its function, i.e., antigenic activity, prophylactic activity and therapeutic activity against meningococcal disease. The specification discloses diagnostic applications, prophylactic applications or therapeutic intentions for the claimed polypeptide. However, the instant specification fails to teach a single variant of a polypeptide sequence having 50 to 99% identity to the amino acid sequence of SEQ ID NO: 1331 and concurrently having the antigenic, diagnostic, prophylactic and therapeutic activity. Diagnostic, prophylactic or therapeutic applications minimally require a specific interaction with a compound, such as an antibody. The precise structure or relevant identifying characteristics of DNA molecules that encode a variant polypeptide having 50-99% identity to the amino acid sequence of SEQ ID NO: 1331 and having the antigenic, diagnostic, prophylactic and the therapeutic functional activities can only be determined empirically by actually making the DNA molecules that encode the polypeptide variants of the recited variability, i.e., the 50-99% sequence identity, and testing the varied DNA molecules to determine whether they encode the 50-99% modified polypeptide variants having the desired antigenic and therapeutic activities. The *Written Description Guidelines* state:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

A mere statement that the invention includes a polypeptide having at least 50% sequence identity to the amino acid sequence of SEQ ID NO: 1331 is insufficient to meet the adequate written description

requirement of the claimed invention. The polypeptide of SEQ ID NO: 1331 has specific biologic properties dictated by the structure of the polypeptide and the corresponding structure of the structural gene sequence which encodes it. A convincing structure-function relationship has to exist between the structure of the gene sequence, the structure of the polypeptide variant encoded, and the function of the encoded polypeptide variant. The function cannot be predicted from the modification of the structure of the gene and in the instant case, the DNA encoding the at least 50% modified polypeptide variant. Applicants have not shown that variation or modification of a reference sequence encoding a polypeptide would automatically predict the production of a polypeptide variant as claimed having the specific antigenic and therapeutic functional activities. The specification fails to teach the structure or relevant identifying characteristics of a representative number of species of DNA molecules encoding a representative number of species of polypeptide variants of at least 50% sequence identity as recited, sufficient to allow one skilled in the art to determine that the inventors had possession of the invention as claimed. With the exception of the polypeptide of SEQ ID NO: 1331, a skilled artisan cannot envision the detailed chemical structure of all the polypeptide variant species encompassed by the recited molecule. Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that its is a part of the invention and a reference to a potential method of isolating it. The polypeptide variant having the specific functions itself is required. See *Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)* and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.*

Rejection(s) under 35 U.S.C. § 112, First Paragraph (Scope of Enablement)

12) Claims 1, 10 and 25-32 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for an isolated fragment of a meningococcal protein wherein the fragment has the amino acid sequence of SEQ ID NO: 1331, does not reasonably provide enablement for a polypeptide comprising a contiguous amino acid sequence with 'at least 50% sequence identity to SEQ ID NO: 1331', wherein the polypeptide comprises at least one antigenic determinant and has a length of 100 amino acids or less, as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Instant claims are evaluated based on *Wands* factors. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

Instant claims encompass a protein fragment comprising a contiguous amino acid sequence with at least 50% sequence identity to a 18 amino acid-long amino acid sequence, SEQ ID NO: 1331, wherein the protein fragment comprises at least one antigenic determinant and has a length of 100 amino acids or less. The specification indicates diagnostic applications as well as therapeutic and vaccination (prophylactic) intentions. See lines 17-19 and 28-30 of page 3; line 13 of page 4 of the specification; section 'Immunodiagnostic Assays' on pages 33 and 34 of the specification; and section 'Vaccines' on pages 23-25 o the specification. The 'antigenic determinant' is described as including B-cell epitopes and T-cell epitopes (see line 7 of page 5 of the specification). The claimed product is required to serve as an agent that treats, ameliorates or prevents a desired disease (see lines 20-25 of page 22 of the specification). In other words, the recited polypeptide variant having at least 50% dissimilarity with the amino acid sequence of SEQ ID NO: 1331 is *required* to have the antigenic, diagnostic, therapeutic and prophylactic activities such that a composition comprising the polypeptide variant can be used to diagnose, treat or prevent meningococcal diseases. However, the instant specification does not teach how to make a polypeptide variant of the amino acid sequence of SEQ ID NO: 1331 with at least 50% of its amino acids varied or modified in such a way that the resultant polypeptide variant still contains a B-cell epitope and a T-cell epitope and retains the antigenic, diagnostic, therapeutic and prophylactic activities of the native polypeptide. Neither the specification nor the art discloses a polypeptide variant that is at least 50% non-identical to the amino acid sequence of the 18 amino acid-long SEQ ID NO: 1331 which variant retains the above-identified required functions. The instant specification fails to demonstrate that a polypeptide variant having at least 50% identity, i.e. at least 50% non-identity to SEQ ID NO: 1331, if prepared by one of skill in

the art using art-known methods, would retain all the functional or biological properties of the native protein from which the fragment, SEQ ID NO: 1331, was obtained, or to the native polypeptide fragment of SEQ ID NO: 1331 itself. It should be noted that predictability or unpredictability is one of the *Wands* factors for enablement. The precise structural composition of the claimed polypeptide variant is not disclosed, without which one of ordinary skill in the art cannot make and use the claimed product in the claimed method without undue experimentation. The specification lacks disclosure as to how to produce a polypeptide variant having at least 50% sequence identity to SEQ ID NO: 1331 and at the same time having all the necessary functions for use as a diagnostic reagent and a therapeutic and a prophylactic agent. There is no evidence within the instant specification showing that the claimed polypeptide variant having an amino acid sequence which is 'at least 50%' sequence identity to the amino acid sequence of the polypeptide of SEQ ID NO: 1331, does in fact have at least one antigenic determinant that contains a B-cell epitope and a T-cell epitope and the required biologic activities. There is no predictability that such a polypeptide variant having as much as 50% dissimilarity with the polypeptide of SEQ ID NO: 1331, would remain functional as an effective diagnostic reagent and an effective therapeutic and a prophylactic agent. This is critical because the art reflects sensitivity of proteins or polypeptides to alteration of even a single amino acid residue in its amino acid sequence. An alteration in a single amino acid can eliminate or drastically change one or more function(s) of the polypeptide. For instance, Burgess *et al* (*J. Cell Biol.* 111: 2129-2138, 1990) taught that replacement of a single lysine residue at position 118 of the protein, acidic fibroblast growth factor, by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similar teachings are provided by Lazar *et al* (*Mol. Cellular Biol.* 8: 1247-1252, 1988), who showed that in the protein, transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity, while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. In the instant case, it is unlikely that a polypeptide molecule having as much as 50% dissimilarity with the 18 amino acid-long native polypeptide of SEQ ID NO: 1331 as recited, would have its primary, secondary or tertiary structure unchanged such that it contains at least one antigenic determinant containing a B-cell epitope and a T-cell epitope and would have the required biologic activities retained. The effects of such a high dissimilarity upon the polypeptide structure and

function are unpredictable. One of skill in the art cannot predict that such a polypeptide variant would have its immunologic or biologic specificity retained. Bowie *et al.* (*Science* 247: 1306-1310, 1990) taught that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome. Bowie *et al.* further taught that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (see column 1 on page 1306). Bowie *et al* also taught that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function(s) is limited. Certain positions in the polypeptide sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (see column 2 on page 1306). Thus, while the art demonstrates that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein or polypeptide, with as much as 50% dissimilarity to the 18 amino acid-long polypeptide fragment of SEQ ID NO: 1331, the therapeutic, prophylactic and diagnostic activities of the claimed polypeptide variant could not be predicted, based solely on the sequence identity, nor would it be expected to be the same as that of the polypeptide fragment of SEQ ID NO: 1331. For example, if one nucleotide in the nucleotide sequence that encodes the polypeptide of SEQ ID NO: 1331 is deleted or inserted at a single position within the coding sequence, all the codons down stream of that insertion or deletion would be frame-shifted. If that frame-shift took place near the 5' end of the gene, it is likely that the polypeptide expressed will have little in common structurally or functionally with the native polypeptide of SEQ ID NO: 1331. There is no certainty that amino acid substitutions at any position would yield a polypeptide variant that retains the function and/or the specificity of the native polypeptide of SEQ ID NO: 1331 or the native protein from which SEQ ID NO: 1331 was obtained. The specification fails to demonstrate that a polypeptide having 50% structural dissimilarity to SEQ ID NO: 1331 would be functionally equivalent to the native polypeptide fragment of SEQ ID NO: 1331 or the native protein from which SEQ ID NO: 1331 was obtained particularly with regard to the therapeutic, prophylactic and diagnostic functions. One simply cannot predict what effects a given

deletion, insertion or modification in the amino acid sequence would cause, and therefore such modified molecules are not enabled as Applicants' invention. Applicants have not enabled the full scope of the invention as claimed for those polypeptide molecules which are altered or varied. The specification only discloses a polypeptide fragment comprising the amino acid sequence of SEQ ID NO: 1331. Undisclosed and unidentified functional polypeptide molecules of at least 50% sequence identity encompassed in the claims are not enabled for their scope. Although a skilled artisan might envision making a number of changes in the reference polypeptide sequence in accordance with Applicants' disclosure, it is highly uncertain that the polypeptide variant as recited would be functionally equivalent to the native unmodified polypeptide. The altered polypeptide would vary in an unknown or unpredictable manner from the disclosed native polypeptide sequence. For these reasons, making and using of the instantly claimed polypeptide variant having the desired function(s) is well outside the realm of routine experimentation. Accordingly, undue experimentation would have been required by one of ordinary skill in the art at the time of the effective filing date of the instant application to reproducibly practice the invention as claimed due to the lack of specific guidance, the lack of enabling disclosure, the art-demonstrated functional unpredictability as reflected in the state of the art, the breadth of the claims, and the quantity of experimentation necessary. The claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

13) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

14) Claims 1, 10 and 25-32 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 1 lacks proper antecedent basis in the limitation: 'SEQ ID NO: 1331' (see lines 3 and 4). Since the claim already includes the limitation, it is suggested that Applicants replace the limitation with --said SEQ ID NO: 1331--.

(b) Claims 10 and 25-32, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base

claim.

Rejection(s) under 35 U.S.C § 102

15) The following is a quotation of the appropriate paragraph(s) of 35 U.S.C. § 102 that form the basis for the rejection(s) under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16) Claims 1 and 25-28 are rejected under 35 U.S.C § 102(b) as being anticipated by Relf *et al.* (*J. Clin. Microbiol.* 30: 3190-3194, 1992).

It is noted that the claimed polypeptide having at least one antigenic determinant encompasses a protein fragment having a length of three amino acids or greater. See original claim 3.

Relf *et al.* disclosed a 59 amino acid-long polypeptide having a contiguous amino acid sequence, KAAELNQKSKELE, with at least 50% sequence identity to the instantly recited SEQ ID NO: 1331. The prior art polypeptide comprises a 5-amino aid-long KAAEN, and a 4-amino acid-long KELE antigenic determinant. See attached sequence alignment report; and Figure 1.

Claims 1 and 25-28 are anticipated by Relf *et al.*

Rejection(s) under 35 U.S.C. § 103

17) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

18) Claims 10 and 29-32 are rejected under 35 U.S.C § 103(a) as being unpatentable over Relf

et al. (*J. Clin. Microbiol.* 30: 3190-3194, 1992) as applied to claim 1 or 25 above.

The teachings of Relf *et al.* are explained above, which do not disclose their composition to be comprising a pharmaceutically acceptable vehicle.

However, it was well known, conventional and routine in the art to add a pharmaceutically acceptable vehicle, such as saline or water, to an art known polypeptide.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add an art known or art available pharmaceutically acceptable vehicle, such as saline or water, to Relf's polypeptide to produce the instant invention, with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Relf's composition in a solution form suitable for further studying the functional or biologic properties of the polypeptide, since it is routine and conventional in the art to do so.

Claims 10 and 29-32 are *prima facie* obvious over the prior art of record.

Remarks

19) Claims 1, 10 and 25-32 stand rejected.

20) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses and papers is (571) 273-8300.

21) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

22) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week,

which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

January, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER

SEQ ID NO. 1331.

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RESULT 6
Q03122
ID   Q03122          PRELIMINARY;      PRT;    59 AA.
AC   Q03122;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   M-like protein (Fragment).
OS   Streptococcus pyogenes.
OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
OC   Streptococcus.
OX   NCBI_TaxID=1314;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93084815; PubMed=1339461;
RA   Relf W.A., Martin D.R., Sriprakash K.S.;
RT   "Identification of sequence types among the M-nontypeable group A
RT   streptococci [see comments].";
RL   J. Clin. Microbiol. 30:3190-3194(1992).
DR   EMBL; L05024; AAA21790.1; -.
FT   NON_TER         1      1
FT   NON_TER        59     59
SQ   SEQUENCE   59 AA;  6996 MW;  FA7A45ADA1A26857 CRC64;

  Query Match             59.1%;  Score 52;  DB 2;  Length 59;
  Best Local Similarity   64.7%;  Pred. No. 3.1;
  Matches   11;  Conservative    2;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 PTQKAAELNQKSKELEQ 17
              | :|||||  | ||||:
Db          7 PVKKAAELYDKIKELEE 23
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